

IN THE CLAIMS

Please replace the claims as filed with the claims set forth below. This listing of claims will replace all prior versions, and listings, of claims in the application:

1. (currently amended) A non-neurovirulent oncolytic herpes simplex virus, wherein the herpes simplex virus genome comprises a nucleic acid encoding an antisense to the squamous cell carcinoma related oncogene (asSCCRO), which squamous cell carcinoma related oncogene comprises the nucleotide sequence of SEQ ID NO: 1 or SEQ ID NO: 3; and

wherein the nucleic acid in the herpes simplex virus genome encodes a nucleotide sequence having at least 90% sequence identity to a nucleotide sequence complementary to:

- (i) the polynucleotide sequence of SEQ ID No. 1 or 3 or its complement; or
- (ii) the mRNA transcript of SEQ ID No. 1 or 3; or
- (iii) a fragment of said polynucleotide sequence or mRNA transcript.

2. (previously presented) The herpes simplex virus according to claim 1 wherein said nucleic acid encodes a mammalian asSCCRO.

3. (previously presented) The herpes simplex virus according to claim 1 wherein said nucleic acid encodes the human asSCCRO.

4. (canceled)

5. (previously presented) The herpes simplex virus according to claim 1 wherein said nucleic acid encodes a nucleotide sequence complementary to:

- (i) the polynucleotide sequence of SEQ ID No. 1 or 3 or its complement;
- (ii) the mRNA transcript of SEQ ID No. 1 or 3; or
- (iii) a fragment of said polynucleotide sequence or mRNA transcript.

6. (canceled)

7. (previously presented) The herpes simplex virus of claim 1 wherein said fragment comprises at least 20 nucleotides and no more than 900 nucleotides.

8. (previously presented) The herpes simplex virus according to claim 1 wherein said nucleic acid hybridizes under high stringency conditions to:

- (i) the polynucleotide sequence of SEQ ID No. 1 or 3 or its complement;
- (ii) the mRNA transcript of SEQ ID No. 1 or 3; or
- (iii) a fragment of said polynucleotide sequence of mRNA transcript.

9. (previously presented) The herpes simplex virus of claim 1 wherein said herpes simplex virus genome further comprises a regulatory sequence operably linked to said nucleic acid encoding an antisense to the squamous cell carcinoma related oncogene (asSCCRO), wherein said regulatory sequence has a role in controlling transcription of said asSCCRO.

10. (previously presented) The herpes simplex virus of claim 1 wherein said nucleic acid is located in at least one RL1 locus of the herpes simplex virus genome.

11. (previously presented) The herpes simplex virus of claim 1 wherein said nucleic acid is located in, or overlaps, at least one of the ICP34.5 protein coding sequences of the herpes virus genome.

12. (previously presented) The herpes simplex virus of claim 1 wherein the herpes simplex virus is a mutant of one of HSV-1 strains 17 or F or HSV-2 strain HG52.

13. (previously presented) The herpes simplex virus of claim 1 wherein the herpes simplex virus is a mutant of HSV-1 strain 17 mutant 1716.

14. (previously presented) The herpes simplex virus of claim 1 which is a gene specific null mutant.

15. (previously presented) The herpes simplex virus of claim 1 which is an ICP34.5 null mutant.

16. (previously presented) The herpes simplex virus of claim 1 which lacks at least one expressible ICP34.5 gene.
17. (previously presented) The herpes simplex virus of claim 1 which lacks only one expressible ICP34.5 gene.
18. (canceled)
19. (previously presented) The herpes simplex virus of claim 1 wherein said nucleic acid encoding the asSCCRO forms part of a nucleic acid cassette integrated in the genome of said herpes simplex virus, said cassette comprising nucleic acid encoding:
 - (a) said as SCCRO; and nucleic acid encoding;
 - (b) a ribosome binding site; and
 - (c) a marker,wherein the nucleic acid encoding asSCCRO is arranged upstream (5') of the nucleic acid encoding asSCCRO, wherein the regulatory nucleotide sequence has a role in regulating transcription of said nucleic acid encoding the asSCCRO.
20. (previously presented) The herpes simplex virus according to claim 19 wherein a regulatory nucleotide sequence is located upstream (5') of the nucleic acid encoding asSCCRO, wherein the regulatory nucleotide sequence has a role in regulating transcription of said nucleic acid encoding the asSCCRO.
21. (previously presented) The herpes simplex virus as claimed in claim 19 wherein the cassette disrupts a protein coding sequence resulting in inactivation of the respective gene product.
22. (previously presented) The herpes simplex virus of claim 19 wherein a transcription product of the cassette is a bi- or poly- cistronic transcript comprising a first cistron encoding the

asSCCRO and a second cistron encoding the marker nucleic acid wherein the ribosome binding site is located between said first and second cistrons.

23. (previously presented) The herpes simplex virus of claim 19 wherein the ribosome binding site comprises an internal ribosome entry site (IRES).

24. (previously presented) The herpes simplex virus of claim 19 wherein the marker is a defined nucleotide sequence encoding a polypeptide.

25. (previously presented) The herpes simplex virus as claimed in claim 24 wherein the marker comprises the Green Fluorescent Protein (GFP) protein coding sequence or the enhanced Green Fluorescent Protein (EGFP) protein coding sequence.

26. (previously presented) The herpes simplex virus of claim 19 wherein the marker comprises a defined nucleotide sequence detectable by hybridization under high stringency conditions with a corresponding labelled nucleic acid probe.

27. (previously presented) The herpes simplex virus of claim 19 wherein the cassette further comprises nucleic acid enclosing a polyadenylation sequence located downstream (3') of the nucleic acid encoding the marker.

28. (previously presented) The herpes simplex virus as claimed in claim 27 wherein the polyadenylation sequence comprises the Simian Virus 40 (SV40) polyadenylation sequence.

29–32. (cancelled)

33. (previously presented) A method of lysing or killing tumour cells *in vitro* or *in vivo* comprising the step of administering to a patient in need of treatment the herpes simplex virus of claim 1.

34. (previously presented) A medicament, pharmaceutical composition or vaccine comprising the herpes simplex virus of claim 1.
35. (previously presented) The medicament, pharmaceutical composition or vaccine as claimed in claim 34 further comprising a pharmaceutically acceptable carrier, adjuvant or diluent.

36. (previously presented) The herpes simplex virus according to claim 1, wherein the nucleic acid sequence is in at least one of the long repeat regions (R₁).

37-41. (cancelled)

42. (currently amended) A method for the treatment of a tumour comprising the step of administering to a patient in need of treatment the herpes simplex virus of claim 36-a non-neurovirulent oncolytic herpes simplex virus, wherein the herpes simplex virus genome comprises a nucleic acid encoding an antisense to the squamous cell carcinoma related oncogene (asSCCRO), which squamous cell carcinoma related oncogene comprises the nucleotide sequence of SEQ ID NO: 1 or SEQ ID NO: 3; and
wherein the nucleic acid in the herpes simplex virus genome encodes a nucleotide sequence having at least 90% sequence identity to a nucleotide sequence complementary to:
(i) the polynucleotide sequence of SEQ ID No. 1 or 3 or its complement; or
(ii) the mRNA transcript of SEQ ID No. 1 or 3; or
(iii) a fragment of said polynucleotide sequence or mRNA transcript, wherein the nucleic acid sequence is in at least one of the long repeat regions (R₁).

43. (cancelled)

44. (previously presented) The method of claim 42 wherein said herpes simplex virus is capable of killing tumour cells.

45. (previously presented) A method of expressing in vitro or in vivo an antisense to the squamous cell carcinoma related oncogene (asSCCRO), said method comprising the step of infecting at least one cell or tissue of interest with the herpes simplex virus of claim 36, wherein asSCCRO is operably linked to a transcription regulatory sequence.

46. (cancelled)

47. (previously presented) The herpes simplex virus of claim 1, wherein the herpes simplex virus is HSV1716asSCCRO (ECACC accession number 04051901).

48-89. (cancelled)

90. (previously presented) A medicament, pharmaceutical composition or vaccine comprising the herpes simplex virus of claim 36.

91. (previously presented) The medicament, pharmaceutical composition or vaccine as claimed in claim 90 further comprising a pharmaceutically acceptable carrier, adjuvant or diluent.

92-94. (cancelled)

95. (previously presented) The herpes simple virus of claim 1, wherein the herpes simplex virus is effective in the treatment of squamous cell cancer.